DETAILED ACTION

Comments

Applicant's amendments and request for reconsideration in the communication filed on 5 April 2011 are acknowledged and the amendments are entered.

Claims 1-10 are pending in the instant application.

Claims 1-10 are examined in this Office action.

Withdrawn Rejections

The rejections of claims 1-10 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter are withdrawn in view of amendments filed to the instant set of claims on 5 April 2011.

The rejections of claims 1-10 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter are withdrawn in view of amendments filed to the instant set of claims on 5 April 2011.

The provisional rejections of claims 1-2, 5-6, and 8-10 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 11/917,452 in view of Christopherson et al. in view of Winokur et al. in view of Higenbottam et al. are withdrawn in view of the terminal disclaimer filed on 5 April 2011.

The provisional rejections of claims 1-2 and 6 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-18 of

copending Application No. 11/569,449 are withdrawn in view of the terminal disclaimer filed on 5 April 2011.

Terminal Disclaimers

The terminal disclaimer filed on 5 April 2011 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 11/569,449 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 5 April 2011 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 11/917,452 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejections are reiterated:

35 U.S.C. 103 Rejection #1:

Claims 1-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. [US Patent 5,944,680; issued 31 August 1999] in view of Winokur et al. [US Patent 5,968,932; issued 19 October 1999] in view of Higenbottam et al. [WO 00/01434; published 13 January 2000] in view of Willmann et al. [Biosilico, volume 1, September 2003, pages 121-124; on IDS].

Claim 1 is drawn to a method for administering a medicament into a body of a patient in need of treatment with the medicament as a function of time with the aid of a computer-controlled dosage device. The method comprises inputting an indication and substance dependent target profile that indicates a desired effect-time profile and a dosage time profile which describes the dose administered as a function of time into a physiology-based and/or pharmacodynamic computer model module. The method also comprises physiology-based pharmacokinetic and/or pharmacodynamic simulating with a time-variable application profile while taking into account individual anatomical and/or physiological parameters of a body to be treated and substance-specific input parameters of the medicament to be administered within the physiology-based and/or

pharmacodynamic computer model module and outputting a simulated time profile. The method also comprises iterative adapting of the dosage time profile until the simulated time profile matches the predetermined target profile. The method additionally comprises outputting of the adapted dosage time profile to control the dosage device according to the adapted dosage time profile, and administering the medicament to the patient using the dosage device controlled by the adapted dosage time profile.

The document of Christopherson et al. is drawn to a respiratory effort detection method [title]. The method is used to correct breathing patterns of humans with respiratory disorders (focusing on sleep apnea) [abstract, cover figure, and column 1, lines 13-21 of Christopherson et al.]. The computer control of the dosage of the voltage into the patient is illustrated in Figure 19 of Christopherson et al.

Specifically, normal (i.e. target) respiration profiles (flow of area through the subject over time) are input into Figure 2 of Christopherson et al. Figure 4C of Christopherson et al. illustrates a respiration profile of a subject with sleep apnea. To correct the profile, the apparatus ("dosage device") illustrated in Figure 5 of Christopherson et al. is implanted into the patient. When the respiratory profile of the subject is abnormal (such as in Figure 4C of Christopherson et al.) column 30, lines 30-35 of Christopherson et al. teach that this device administers a dose of voltage that is optimized over several trials (i.e. iterations) to correct the abnormal respiratory profile to maximize agreement with the normal respiratory profile (as output in Figure 4A and Figure 4B of Christopherson et al.).

However, Christopherson et al. does not teach use of a medicament (instead, Christopherson et al. uses dosages of electric voltages to resolve sleep apnea). Also, Christopherson et al. does not teach using simulations to model a diseased subject using physiology-based pharmacokinetic profiling (instead, Christopherson et al. obtained the diseased respiratory profile empirically).

The document of Winokur et al. alternatively inhibits sleep apnea with the medicament of the pharmaceutical salt of 6-methyl-5-oxo-3-thiomorpholinylcarbonyl-L-histidine-L-prolinamide [title and abstract]. Column 3, lines 20-40 of Winokur et al. teach inhalation of Montirelin.

However, Winokur et al. does not teach automated administration of the chemical medicament to the patient.

The document of Higenbottam et al. studies inhalers [title]. In particular, the cover figure and abstract of Higenbottam et al. demonstrate the structure and function of an automated inhaler that administers a chemical to the trachea and lungs [Figure 2 of Higenbottam et al.) as needed.

Christopherson et al., Winokur et al. and Higenbottam et al. do not teach using simulations to model a diseased subject using physiology-based pharmacokinetic profiling (instead, Christopherson et al. obtained the diseased respiratory profile empirically).

The article of Willmann et al. teaches the simulation software "PK-Sim," a physiologically based pharmacokinetic "whole body" modeling algorithm. Specifically, Figure 1 on page 122 of Willmann et al. illustrates that to determine the effect of a

medicine on the (in this case) human body, the human body is computationally decomposed into a series of connected boxes, wherein each box represents an organ or bloodpool. Differential equations are used to model the kinetics of the profile of the medicine through the iteratively connected boxes as a function of time using a series of empirically obtained parameters.

With regard to claim 2, the cover figure of Christopherson et al. and Figure 1 of Willmann et al. illustrates that the dosage device and simulation is applicable to administering the voltages to humans. Claim 1 of Winokur et al. indicates that their medicament for sleep apnea is applicable to mammals.

With regard to claim 3, column 2, lines 20-30 of Winokur et al. teach intravenous and oral dosages of Montirelin (6-methyl-5-oxo-3-thiomorpholinylcarbonyl-L-histidine-L-prolinamide) to treat sleep apnea. Additionally, column 3, lines 20-40 of Winokur et al. teaches inhalation of Montirelin.

With regard to claim 4, Figure 1 of Christopherson et al. illustrates the volume and composition of a throat and trachea that are normal. Figure 3 of Christopherson et al. illustrates the volume and composition of a throat and trachea that are diseased with sleep apnea. With regard to claims 8-9, the respiratory profiles in Figures 2 and 4 of Christopherson et al. are measured physiologically by the apparatus anatomically positioned in the human in Figure 5 as the subject breathes (real-time).

With regard to claim 7, the device infused into the human in Figure 5 of Christopherson et al. pumps voltage into the human respiration pathway to correct for abnormal respiration profiles.

With regard to claim 10, the therapy in Christopherson et al. is evaluated by measuring pressure through the measurement probe of a pressure sensor (Figure 6 of Christopherson et al.) to determine the signal of intensity of air flow. Additionally, the resultant signal (whether it be normal as in Figure 2 of Christopherson et al. or abnormal as in Figure 4C of Christopherson et al.) controls whether the dosage of voltage in given by the apparatus to clear the pathway.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the implanted device that applied voltages to treat sleep apnea as in Christopherson et al. by use of administering the medicament Montirelin as in Winokur et al. wherein the motivation would have been that the use of the pharmaceutical in Winokur et al. is non-invasive (i.e. no devices need to be implanted-column 2, lines 20-30 of Winokur et al. and column 3, lines 20-40 of Winokur et al. as compared with Figure 5 of Christopherson et al). There would have been a reasonable expectation of success in combining Christopherson et al. with Winokur et al. because both studies pertain to applying optimized dosages (i.e. electricity or chemicals) for treating sleep apnea when abnormal breathing patterns occur. In addition, it has been

shown in Higenbottam et al. that there is success in automated dosing of chemicals to the trachea and lungs [Figures 1 and 2 of Higenbottam et al.].

It would have been further obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invasive and noninvasive approaches of administering dosages in Christopherson et al., Winokur et al., and Higenbottam et al., by use of the computational simulation for the "whole body" as in Willmann et al. wherein the motivation would have been that computational simulation of dosage performance eliminates the need to administer dosages to a subject- invasively or noninvasively- until optimized conditions have been modeled [Figures 1 and 2 of Willmann et al.]. There would have been a reasonable expectation of success in combining the general study of Willmann et al. to the specific assessment of sleep apnea in Christopherson et al., Winokur et al., and Higenbottam et al. because as the simulations of Willmann et al. are applicable to the "whole body "[title], and the throat and trachea are parts of the body, Willmann et al. provides generally applicable simulated results to the documents of Christopherson et al. and Winokur et al.

Response to arguments:

Applicant's arguments filed 5 April 2011 have been fully considered but they are not persuasive.

Applicant argues on pages 8-9 of the Remarks that there is no advantage or reasonable expectation of success in combining the implanted device administering voltages of Christopherson et al. with the bolus injection of Montirelin of Winokur et al.

This argument is not persuasive because it does not take into account all of the references in the rejection. While Winokur et al. teaches inhalation of Montirelin for sleep apnea, and while Christopherson et al. teaches automated dosaging of voltages in the respiratory tract to also control sleep apnea; the references of Higgenbottam et al. (not directly addressed in the Remarks) teaches an electronic and automated inhaler that administers chemicals to the respiratory tract. Consequently, the combination of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. make obvious two alternative forms of delivering dosages to the trachea: the first method is by delivering dosages of voltages to the trachea; the second method is electronically delivering Montirelin to the respiratory tract through an automated inhaler. There would have been a reasonable expectation of success in combining Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. because the combination of references analogously pertains to understanding the delivery of drugs or voltages to the respiratory tract to better comprehend or simulate sleep apnea.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #2:

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Higenbottam et al. in view of Willmann et al. as applied to claims 1-4 and 7-10 above, in further view of Sugita et al. [US PGPUB 2003/0175350 A1; published 18 September 2003].

Claim 5 is further limiting accounting for the substance specific parameter of free fraction of the medicament in plasma.

The documents of Christopherson et al., Winokur et al., Higenbottam et al. and Willmann et al. make obvious methods for determining the controlled dosage of a medicament, as discussed above. The abstract of Winokur et al. teaches use of the drug Montirelin to treat sleep apnea.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. do not teach the property of free fraction of the Montirelin in blood plasma.

The document of Sugita et al. teaches preparation and characterization of thyrotropin-releasing hormones and their derivatives [title, abstract]. Paragraph 5 of Sugita et al. teaches that Montirelin is a derivative of thyrotropin-releasing hormones. Paragraph 49 of Sugita et al. teaches the process for measuring blood plasma levels of thyrotropin-releasing hormones and their derivatives.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical and computational determination of controlled dosage of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. by use of the blood plasma measurement techniques for Montirelin in Sugita et al, wherein the motivation would have been that the result of Sugita et al. yields information on how much Montirelin is capable of dissolving in the bloodstream.

Response to arguments:

Applicant's arguments filed 5 April 2011 have been fully considered but they are not persuasive.

Applicant argues that the reference of Sugita et al. does not overcome the alleged deficiencies of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. This argument is not persuasive because the combination of Christopherson et al., Winokur et al., Higenbottam et al., Willmann et al., and Sugita et al. makes obvious all of the limitations of the instantly rejected claim.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #3:

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Higenbottam et al., in view of Willmann et al. as applied to claims 1-4 and 7-10 above, in further view of Numerical Modeling [Definition of Numerical Modelling, 2000, The Dictionary of Physical Geography].

Claim 6 is further limiting wherein numerical optimization methods comprise gradient and stochastic methods.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. make obvious methods for determining the controlled dosage of a medicament, as discussed above. Figure 1 of Willmann et al. suggests a system of differential equations needed to model the pharmacokinetics of a medicament when administered to the body.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. do not teach gradient and stochastic methods for optimizing dosages.

The article on Numerical Modeling teaches that gradients and stochastic analyses forms of techniques used to model differential equations [see definition].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical and computational determination of controlled dosage of Christopherson et al., Winokur et al., Higenbottam et al. and Willmann et al. by use of the mathematical techniques in Numerical modeling because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the stochastic and gradient techniques are alternate techniques used to solve differential equations. There would have been a reasonable expectation of success in combining the techniques of Numerical modeling with the differential equations in the dosage studies of the combination of Christopherson et al., Winokur et al., and Willmann et al. because the Numerical modeling taught in the definition is general for any system of differential equations (including the differential equations on Willmann et al.).

Response to arguments:

Applicant's arguments filed 5 April 2011 have been fully considered but they are not persuasive.

Applicant argues that the reference of Numerical Modelling does not overcome the alleged deficiencies of Christopherson et al., Winokur et al., Higenbottam et al., and

Willmann et al. This argument is not persuasive because the combination of Christopherson et al., Winokur et al., Higenbottam et al., Willmann et al., and Numerical Modelling makes obvious all of the limitations of the instantly rejected claim.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Russell S. Negin/
Primary Examiner, Art Unit 1631
3 June 2011